ORIGINAL RESEARCH PAPER
Volume-6 | Issue-10 | October-2017 | ISSN No 2277 - 8179 | IF : 4.176 | IC Value : 78.46
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

DENTAL PULP STEM CELLS

Dental Science

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ABSTRACT

Aim: The aim of this review is to study about the dental pulp stem cells and its implications in dentistry.

Background: Stem cells are found inside the soft living tissue. Dental pulp is the soft living tissue inside a tooth. Scientists have identified the mesenchymal type of stem cell inside dental pulp. Dental Pulp Stem Cells, or (DPSCs) are multipotent stem cells that have the potential to differentiate into a variety of cell types. There are various studies where the importance of these cells and their regenerative capacity has been demonstrated. Through the addition of tissue-specific cytokines, differentiated cells were obtained in vitro from these cells, not only of mesenchymal linage but also of endo and ectodermal linage.

Reason: The regenerative ability of dental pulp stem cells make them a important field in the field of research. This review is a brief insight about dental pulp stem cells.

KEYWORDS

INTRODUCTION:

Regenerative medicine is a branch of translational research in tissue engineering and molecular biology which deals with the process of replacing, regenerating and engineering human cells, tissues or organs in order to restore or establish normal function. Stem cells, progenitor cells that can give rise to a variety of tissues play an important role in this endeavor. Stem cells are undifferentiated , biological cells that can differentiate into specialized cells, undergo multiplication to form a new group of cells. Bone marrow, adipose tissue and blood are the most commonly used sources of stem cells in mammals. Recently, stem cells from umbilical cord blood and dental pulp are also being harvested. Dental pulp is the soft tissue found inside the tooth, derived from migrating neural crest cells during development [1,2] . Dental pulp stem cells (DPSCs) are a promising source of cells for numerous and varied regenerative applications. Their natural function in the production of odontoblasts to create reparative dentin support applications in dentistry in the regeneration of tooth structures. They are also being investigated for the repair of tissues outside of the tooth. The ease of isolation of DPSCs from discarded or removed teeth offers a promising source of autologous cells, and their similarities with bone marrow stromal cells (BMSCs) suggest applications in musculoskeletal regenerative medicine. DPSCs are derived from the neural crest and, therefore, have a different developmental origin to BMSCs. These differences from BMSCs in origin and phenotype are being exploited in neurological and other applications. This review throws an insight into the isolation, regeneration and application of DPSCs in regenerative medicine.

Physiology of dental pulp:

The tooth is developed from the tooth germ which is derived from the ectoderm of first pharyngeal arch and ectomesenchyme of the neural crest cells. It mainly consists of enamel organ, dental papilla and dental sac. The tooth has enamel derived from the ameloblasts, dentin from the odontoblasts and the innermost region the pulp. The pulp consists of blood vessels, connective tissue, lymphatic and nerve supply. After the cusp formation the enamel undergoes programmed cell death losing its ability to repair enamel. Reparative dentin is formed from the migrating stem cells forming odontoblasts, which is derived from the dental pulp. (5,6,7)

Role of dental pulp in reparative dentin formation :

The regeneration of these cells occurs in response to injury, resembling the developmental events of the tooth, with a lesser degree of regulatory control (8). The main cell involved in the regeneration of the dentin is the odontoblasts, which has an active synthetic and secretory role in the primary dentinogenesis stage. These cells are significantly down regulated in the secondary dentinogenesis stage becoming quiescent, slowly secreting secondary dentin. On injury, these cells gets up regulated secreting a tertiary dentin matrix to repair and regenerate the tissue and thereby restoring the tooth integrity.

Reactionary dentin is seen in response to lesser intensity injury such as early caries, tooth wear, etc.., where dentin matrix is secreted by the primary odontoblasts. In case of severe injury, odontoblast-like cells differentiate from the stem cells within the pulp and secrete reparative dentin matrix(9), its more complex when compared to the formation of reactionary dentinal matrix. Since the reparative dentin has a pathological nature of secretion they are variable in the degree of tubularity, which has its consequence in the permeability(10). Whereas the physiological dentin has a tight control of events to the odontoblast differentiation which will not necessarily be replicated during reparative dentinogenesis.(11).

Isolation of dental pulp stem cells:

The fundament in isolation is the enzymatic digestion of tissue followed by the growth of the isolated cells in a medium(12,13). Isolated immature stem cells involve a multi step approach. The stem cells are identified using a series of in vitro tests. Colony-forming assays to confirm clonogenecity, phenotypic assays to evaluate cell morphology and cell behavior, flow cytometry to evaluate the surface markers found on the cells in representative tissues. They also confirm the multipotency of dental pulp stem cells by the evidence of odontoblast like differentiation, chondrogenic differentiation and neurogenic differentiation.(14-23). In vivo functional assays are used to confirm if the implanted stem cells in the new environment successfully integrate with adjacent cells, survive and differentiate(24) Stem cells can be isolated from the permanent tooth, exfoliated primary tooth the incisors and the canines, molars cannot be used as they take a longer time for the root to resorb and by the time it is impossible to extract stem cells from the pulpal tissues. (25-27)

Various type of stem cells can be obtained from the tooth, they are the adipocytes used to treat various spine and orthopedic conditions, Crohn's disease, cardiovascular diseases and may also be useful in plastic surgery[28], the chondrocytes and osteoblasts which have been used to grow intact teeth in animals, mesenchymal stem cells (MSCs), have successfully been used to repair spinal cord injury and to restore feeling and movement in paralyzed human patients. They can also be used to treat neuronal degenerative disorders such as Parkinson's disease, cerebral palsy, Alzheimer's disease, and other such disorders. MSCs have better curative potential than other type of adult stem cells.(29)

Applications of dental pulp stem cells in bone regeneration:

Neural induction of DPSCs In Vivo:

To study the neuronal differentiation capacity of DPSCs during a time of active neurogenesis an in vivo developmental avian embryo model was adapted(30). The study was conducted by injecting GFP-expressing DPSCs and control human foreskin fibroblasts (HFFs) into regions adjacent to the developing neural tube at developmental stages, when the CNC cells coalese, migrate to their target tissue, and differentiate into neural derivatives (31). DPSCs were detected using

antibodies to GFP. The neuronal differentiation of transplanted DPSCs and HFFs were investigated at 24, 48 and 72 hours after injection. Human origin of the injected DPSCs where confirmed by staining the embryos with human-specific integrin antibody 48 hours after injection. At 24 hours, DPSCs showed extended processes but did not co localize with neuronal-specific markers. At 48 hours the response of DPSCs where more pronounced, where they resembled the morphology of bipolar cells and neurons with multiple neuritis, which appeared to have migrated into the central nervous system based on merged z-series confocal analysis. The ones which displayed the multiple neurite morphology co localized with both early and mature neural markers. At 72 hours after injection, DPSCs displayed bipolar processes when in close proximity to endogenous sensory axons, exhibited multineurite processes when localized to the central nervous system. Seven days after the injection , DPSCs where still viable as demonstrated with integrin antibody staining of frozen sections. In order to verify if these reactions where common for all ectodermal derived or if they where specific to DPSCs , HFFs was used as a control(32). This potential of the DPSCs can be incorporated in treatment of central nervous system disorders, peripheral nerve injury, stroke, spinal cord injury, etc..,(33-36)

Angiogenesis and Vasculogenesis:

Human DPSCs were able to repair the infarcted myocardium, with an observed increase in number of vessels and reduction of infarct size; this was likely due to secretion of paracrine factors, such as VEGF.(37) A highly vasculogenic population of cells was isolated from dental pulp These cells expressed CD34 and VEGFR2 and formed extensive networks of cords and tube-like structures demonstrating neo vascularization ability. Local

Transplantation of this sub fraction in a mouse hind-limb ischaemia model resulted in successful engraftment and increase in blood flow including high density of capillary formation (38). DPSCs induced paracrine-mediated angiogenesis has also been demonstrated (39). DPSCs produced high amounts of angiogenic molecules, stimulated endothelial cell migration by activation of the P13l–AKT and MEK–ERK pathways and significantly induced the formation of blood vessels in a chicken chorioallantoic membrane model providing evidence of the suitability of DPSCs for treatment of pathologies correlated with inadequate angiogenesis. This potential of DPSCs can be used in the treatment of myocardial infarction and ischemia

Endocrinology:

DPSCs have been differentiated to produce hepatocyte-like cells (HLCs) with acquired hepatocyte functions, such as glycogen storage and urea production (40, 41). Hepatic differentiation of cryopreserved DPSCs was undertaken; the differentiated cells possessed a polygonal shape and normal karyotype and expressed hepatic metabolic function genes and liver specific genes. Glycogen storage and urea production indicated that DPSCs differentiated cells closely resemble HLCs (42). The potential of DPSCs to differentiate into pancreatic cell lineage resembling islet-like cell aggregates (ICAs) has been explored, with the result that in vitro ICAs glucose-dependently released insulin and C-peptide (43). DPSC under appropriate stimuli has shown to express genes related to pancreatic β-cell development and function, including insulin and pancreatic and duodenal homebox-1 (44). DPSCs is a promising source in the treatment of liver failure and diabetes.

Conclusion:

Dental pulp stem cells is recent advancement in regenerative field. DPSCs can be easily obtained from tooth that is naturally lost during childhood or tooth that is surgically removed due impaction. It is used for multiple purposes and has its limitations such as immunologic rejection, difficulty to isolate and grow these cells in labs and potential oncogenic reactions is to be determined. Proper isolation and multiplication of these cells can give different lineage of cells which adds up to the advantages of these cells. On eliminating the risk factors, DSPCs can be used for multiple purposes in medical and dental field.

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